Amendments to the Claims

Please amend claims 27-32, 34, 62, 63, 72 and 73. Please add new claims 74-80. Please cancel claims 35 and 60 without prejudice. This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1-26 (cancelled)

27. (currently amended) A method for designing an optimized multi-epitope polypeptide comprising:

(i) selecting two or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class I cytotoxic T lymphocyte (CTL) epitopes; and

(ii) incorporating said two or more CTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

~~(a) a~~ at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitopes; wherein said flanking or spacer amino acid residue is selected from the group consisting of lysine (K), arginine (R), asparagine (N), glutamine (Q), glycine (G), alanine (A), serine (S), cysteine (C), and threonine (T); and

~~(b) a spacer is introduced between those epitopes of said two or more CTL epitopes that form a junctional epitope when placed adjacent to each other.~~ wherein said

flanking or spacer amino acid residue prevents the occurrence of a CTL junctional epitope.

28. (currently amended) A method for designing an optimized multi-epitope polypeptide comprising:

(i) selecting two or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class II helper T lymphocyte (HTL) epitopes; and

(ii) incorporating said two or more HTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

~~(a) a~~ at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitopes; wherein said flanking or spacer amino acid residue is selected from the group consisting of G, proline (P), N or A; and

~~(b) a spacer is introduced between those epitopes of said two or more HTL epitopes that form a junctional epitope when placed adjacent to each other.~~ wherein said flanking or spacer amino acid residue prevents the occurrence of an HTL junctional epitope.

29. (currently amended) The method of claim 28, wherein said flanking or [[the]] spacer amino acid residues are independently selected from residues that are not known human leukocyte antigen (HLA) Class II primary anchor residues.

30. (currently amended) The method of claim 28, wherein ~~introducing the spacer residues prevents the occurrence of an HTL epitope and further, wherein a~~ said flanking or spacer amino acid residues comprise ~~comprises~~ at least 5 amino acid residues independently selected from the group consisting of G, P, and N.

31. (currently amended) The method of claim 30, wherein [[the]] said flanking or spacer amino acid residues are [[is]] GPGPG (SEQ ID NO: 369).

32. (currently amended) The method of claim 27, wherein ~~introducing the spacer residues prevents the occurrence of an HTL epitope and further, wherein the~~ said flanking or spacer amino acid residues comprise [[is]] 1, 2, 3, 4, 5, 6, 7, or 8 amino acid residues selected from the group consisting of A and G.

33. (cancelled)

34. (currently amended) The method of claim 27, wherein [[the]] said flanking or spacer amino acid residues are ~~residue is~~ selected from the group consisting of K, R, N, G, and A.

35. (cancelled)

36. (previously presented) The method of claim 27, further comprising substituting an N-terminal residue of an HLA epitope that is adjacent to a C-terminus of an HLA epitope comprised by the multi-epitope polypeptide with a residue selected from the group consisting of K, R, N, G, and A.

37-57. (cancelled)

58. (previously presented) The method of claim 27, further comprising initially sorting the epitopes to be incorporated into the multi-epitope polypeptide to provide an order that minimizes the number of junctional epitopes formed.

59. (previously presented) The method of claim 27, further comprising:

(i) introducing the multi-epitope polypeptide into a cell; and

(ii) determining that the multi-epitope polypeptide is processed by an HLA processing pathway such that all of the epitopes included in the multi-epitope polypeptide are produced by an HLA processing pathway.

60. (cancelled)

61. (previously presented) The method of claim 28, further comprising initially sorting the epitopes to be incorporated into the multi-epitope polypeptide to provide an order that minimizes the number of junctional epitopes formed.

62. (currently amended) The method of claim 27, further comprising:

(i) selecting two or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class II helper T lymphocyte (HTL) epitopes; and

(ii) incorporating said two or more HTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

~~(a) a~~ at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitopes; wherein said flanking or spacer amino acid residue is selected from the group consisting of G, P, N or A; and

~~(b) a spacer is introduced between those epitopes of said two or more HTL epitopes that form a junctional epitope when placed adjacent to each other.~~ wherein said flanking or spacer amino acid residue prevents the occurrence of an HTL junctional epitope.

63. (currently amended) The method of claim 28, further comprising:

(i) selecting two or more epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class I cytotoxic T lymphocyte (CTL) epitopes; and

(ii) incorporating said two or more CTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step (ii):

~~(a) a~~ at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitopes; wherein said flanking or

spacer amino acid residue is selected from the group consisting of K, R, N, Q, G, A, S, C, and T; and

~~(b) a spacer is introduced between those epitopes of said two or more CTL epitopes that form a junctional epitope when placed adjacent to each other.~~ wherein said flanking or spacer amino acid residue prevents the occurrence of a CTL junctional epitope.

64. (previously presented) The method of claim 27, wherein said multi-epitope polypeptide contains 10 or more CTL epitopes.

65. (previously presented) The method of claim 64, wherein said multi-epitope polypeptide contains 20 or more CTL epitopes.

66. (previously presented) The method of claim 65, wherein said multi-epitope polypeptide contains 30 or more CTL epitopes.

67. (previously presented) The method of claim 66, wherein said multi-epitope polypeptide contains 40 or more CTL epitopes.

68. (previously presented) The method of claim 28, wherein said multi-epitope polypeptide contains 10 or more HTL epitopes.

69. (previously presented) The method of claim 68, wherein said multi-epitope polypeptide contains 20 or more HTL epitopes.

70. (previously presented) The method of claim 69, wherein said multi-epitope polypeptide contains 30 or more HTL epitopes.

71. (previously presented) The method of claim 70, wherein said multi-epitope polypeptide contains 40 or more HTL epitopes.

72. (currently amended) A method for designing a polynucleotide encoding an optimized multi-epitope polypeptide comprising:

(i) selecting two or more nucleic acid sequences which encode epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class I cytotoxic T lymphocyte (CTL) epitopes ~~epitope nucleic acids~~; and

(ii) incorporating said two or more CTL epitope-encoding nucleic acid sequences ~~acids~~ into a multi-epitope polynucleotide, wherein, during the incorporation step (ii):

[[(a)]] a polynucleotide encoding [[a]] at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitope-encoding nucleic acid sequences ~~acids~~; wherein said flanking or spacer amino acid residue is selected from the group consisting of K, R, N, Q, G, A, S, C, and T; and

~~(b) a polynucleotide encoding a spacer is introduced between those epitopes of said two or more CTL epitope nucleic acids that form a junctional epitope when placed~~

~~adjacent to each other.~~ wherein said flanking or spacer amino acid residue prevents the occurrence of a CTL junctional epitope.

73. (currently amended) A method for designing a polynucleotide encoding an optimized multi-epitope polypeptide comprising:

(i) selecting two or more nucleic acid sequences which encode epitopes that contain human leukocyte antigen (HLA) allele-specific motifs or supermotifs, wherein said epitopes are HLA class II helper T lymphocyte (HTL) epitopes ~~epitope nucleic acids~~; and

(ii) incorporating said two or more HTL epitope-encoding nucleic acid sequences ~~acids~~ into a multi-epitope polynucleotide ~~polypeptide~~, wherein, during the incorporation step (ii):

[[(a)]] a polynucleotide encoding at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitope-encoding nucleic acid sequences ~~acids~~; wherein said flanking or spacer amino acid residue is selected from the group consisting of G, P, N or A; and

~~(b) a polynucleotide encoding a spacer is introduced between those epitopes of said two or more HTL epitope nucleic acids that form a junctional epitope when placed adjacent to each other.~~ wherein said flanking or spacer amino acid prevents the occurrence of an HTL junctional epitope.

74. (new) The method of claim 28, further comprising:

(i) introducing the multi-epitope polypeptide into a cell; and

(ii) determining that the multi-epitope polypeptide is processed by an HLA processing pathway such that all of the epitopes included in the multi-epitope polypeptide are produced by an HLA processing pathway.

75. (new) The method of claim 62, further comprising:

incorporating said two or more CTL epitopes and said two or more HTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step, a spacer is introduced between said two or more CTL epitopes and said two or more HTL epitopes, wherein said spacer prevents the occurrence of a CTL/HTL junctional epitope.

76. (new) The method of claim 63, further comprising:

incorporating said two or more HTL epitopes and said two or more CTL epitopes into a multi-epitope polypeptide, wherein, during the incorporation step, a spacer is introduced between said two or more HTL epitopes and said two or more CTL epitopes, wherein said spacer prevents the occurrence of a CTL/HTL junctional epitope.

77. (new) The method of claim 72, further comprising:

(i) selecting two or more nucleic acid sequences which encode epitopes that contain HLA allele-specific motifs or supermotifs, wherein said epitopes are human leukocyte antigen (HLA) class II helper T lymphocyte (HTL) epitopes; and

(ii) incorporating said two or more HTL epitope-encoding nucleic acid sequences into a multi-epitope polynucleotide, wherein, during the incorporation step (ii):

a polynucleotide encoding at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more HTL epitope-encoding nucleic acid sequences; wherein said flanking or spacer amino acid residue is selected from the group consisting of G, P, N or A; and wherein said flanking or spacer amino acid residue prevents the occurrence of an HTL junctional epitope.

78. (new) The method of claim 73, further comprising:

(i) selecting two or more nucleic acid sequences which encode epitopes that contain HLA allele-specific motifs or supermotifs, wherein said epitopes are human leukocyte antigen (HLA) class I helper T lymphocyte (CTL) epitopes; and

(ii) incorporating said two or more CTL epitope-encoding nucleic acid sequences into a multi-epitope polynucleotide, wherein, during the incorporation step (ii):

a polynucleotide encoding at least one flanking or spacer amino acid residue is introduced at the C-terminus of one or more of said two or more CTL epitope-encoding nucleic acid sequences; wherein said flanking or spacer amino acid residue is selected from the group consisting of K, R, N, Q, G, A, S, C, and T; and wherein said flanking or spacer amino acid prevents the occurrence of a CTL junctional epitope.

79. (new) The method of claim 77, further comprising:

incorporating said two or more CTL epitope-encoding nucleic acid sequences and said two or more HTL epitope-encoding nucleic acid sequences into a multi-epitope polypeptide, wherein, during the incorporation step, a polynucleotide encoding a spacer is introduced between said two or more CTL epitope-encoding nucleic acid sequences and said two or more HTL epitope-encoding nucleic acid sequences, and wherein said spacer prevents the occurrence of a CTL/HTL junctional epitope.

80. (new) The method of claim 78, further comprising:

incorporating said two or more HTL epitope-encoding nucleic acid sequences and said two or more CTL epitope-encoding nucleic acid sequences into a multi-epitope polypeptide, wherein, during the incorporation step, a polynucleotide encoding a spacer is introduced between said two or more HTL epitope-encoding nucleic acid sequences and said two or more CTL epitope-encoding nucleic acid sequences, and wherein said spacer prevents the occurrence of a CTL/HTL junctional epitope.